DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
1401 Rockville Pike
Rockville MD 20852-1448

DEC 30 1998

Our Reference Number: 97-0114
97-0896

Jean-Claude Vincent-Falquet, Pharm. D.
Pasteur Merieux Serums et Vaccins, S.A.
58 Avenue Leclerc
69007 Lyon, France

Dear Dr. Falquet:

Enclosed please find U.S. License 384 issued in accordance with the provisions of Section 351(a) of the Public Health Service Act, as amended November 21, 1997 (FDAMA; Public Law 105-115). This license authorizes Pasteur Merieux Serums et Vaccins, S.A. to manufacture and introduce into interstate and foreign commerce Anti-thymoctye Globulin (Rabbit) for which your company has demonstrated compliance with establishment and product standards. Anti-thymoctye Globulin (Rabbit) is indicated for use in the treatment of acute rejection in renal transplant patients.

Under this license you are authorized to introduce into interstate and foreign commerce Anti-thymoctye Globulin (Rabbit) in 25 mg per container. Change to the product, production process, location of production process, equipment, facilities, or responsible personnel is required to be reported to FDA as specified in Title 21 Code of Federal Regulations (CFR) Section 601.12.

The dating period for this product shall be 24 months from the date of manufacture when stored at 2-8° C. The date of manufacture shall be defined as the date of the first sterile filtration. Results of ongoing stability studies should be submitted throughout the dating period as they become available.

We acknowledge the following actions you have committed to take following licensure of Anti-thymoctye Globulin (Rabbit):

1. Conduct a study to validate the removal/inactivation of the following viruses: HIV1, HIV2, PRV, Poliovirus type 1, Sindbis virus, and a parvovirus; please submit the results of this study as a PLA supplement when it is complete.

2. Use only chemical raw materials which have been tested using U.S. Pharmacopeial methods and meeting USP standards, where such standards exist, the estimated date of implementation to be January 1999; please notify CBER when the changeover is completed.

3. Reprocess bulk product, to reduce endotoxins by addition of [redacted]

4. Perform a study to validate control of bacterial growth in [redacted] treated RBC [redacted] lease submit the results of the study when it is complete.

5. Institute, for every column run, bioburden monitoring of the ion exchange column storage solution, to ensure that storage conditions and storage buffer routinely maintain a bacteriostatic effect.

6. Maintain a maximum limit for [redacted] in final product of [redacted]

7. Maintain a maximum limit for [redacted] in final product of [redacted]

We acknowledge your written commitments dated April 30, June 2, September 11, October 2, November 6, 1998, and November 18, 1998 to include the following facility-related items:

1. Perform a stability study and submit data to support the storage period of up to [redacted] for the final bulk product on the next three lots of product. The stability study protocol and data will be submitted by December 31, 1998.

2. Perform the Rabbit Pyrogen test in compliance with the United States Pharmacopeia (USP).

3. Establish the routine bioburden monitoring alert and action limits for the production process at [redacted], respectively, and reevaluate these limits based on historical data collected after a 90-day bioburden monitoring period.

4. Perform conductivity measurements and submit data on equipment used during the next three batches of product in order to demonstrate that the final rinse water meets the USP conductivity specification for Purified Water. The report and data will be submitted by January 15, 1999.

5. Conduct a cleaning validation study to include total [redacted] assay on the [redacted] tanks, and red blood cell (RBC) treatment vessels, and the [redacted] assay on the RBC treatment vessel for three consecutive batches of product. Collect and report actual data generated during this cleaning validation study and reevaluate the specifications for each assay. This study protocol and data will be submitted by January 15, 1999.

All adverse reports should be submitted according to 21 CFR 600.80 to the Center for Biologics Evaluation and Research (CBER), HFM-210, Food and Drug Administration, 1401 Rockville Pike, Rockville, Maryland 20852-1448. In addition, safety related information obtained in the course of other relevant clinical studies should be reported in accordance with 21 CFR 312.32. It is also requested that distribution reports be submitted according to 21 CFR 600.81.

Please submit three (3) copies of final printed labeling at the time of use accompanied by Part II of Form FDA 2567 with completed implementation information. In addition, you may wish to submit your proposed introductory advertising and promotional campaign. If so, please submit three (3) copies of the proposed material in draft form with Part I of the Form FDA 2567 to CBER, Advertising and Promotional Labeling Staff (APLS), HFM-602, 1401 Rockville Pike, Rockville, Maryland 20852-1448. Promotional claims should be consistent with and not contrary to the approved labeling. No comparative claims or claims of superiority over other similar products should be made unless data to support such claims are submitted to and approved by the Center for Biologics Evaluation and Research. Final copies of advertising and promotional materials should be submitted at the time of use with Part II of Form FDA 2567 to APLS. Please include copies of the approved labeling with your proposed or final copy of advertising and promotional materials submitted to CBER.

Please acknowledge receipt of the enclosed Biologics License to the Director, Division of Blood Applications, HFM-370, Center for Biologics Evaluation and Research, 1401 Rockville Pike, Rockville, Maryland 20852-1448.

Sincerely yours,

Jay S. Epstein, M.D.
Director
Office of Blood Research and Review
Center for Biologics Evaluation
and Research

for Steven Masiello
Director
Office of Compliance
and Biologics Quality
Center for Biologics Evaluation
and Research